Office Action Summary	Application No.	Applicant(s)	
	09/990,909	FALLON, JOAN M.	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7 and 30-67* is/are pending in the application.

4a) Of the above claim(s) *30-35,39-44,50-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7,36-38,45-49 and 56-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/2010*.

4)☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *attached*.

5)☐ Notice of Informal Patent Application.

6)☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 7, and 30-64 and new claims 65-67 are pending in the present application.

Claims 30-35, 39-44, and 50-55 are drawn to non-elected species of invention.

Claims 1, 2, 7, 36-38, 45-49, and 56-64 and 65-67 are under consideration.

Priority

1. This application repeats a substantial portion of prior Application No. 60/249,239, filed November 16, 2000, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it constitutes a continuation-in-part of the provisional application. *Campylobacter and Clostridium difficile do not evidence original descriptive support in the provisional application* therefore claims which recite this combination of claim limitations evidence a priority date of the instant Application which is **November 16, 2001**.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on August 10, 2010 is substantially in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Withdrawn Objections/Rejections

2. **Withdrawn**, The specification objected to as failing to provide proper antecedent basis for the claimed subject matter is herein withdrawn in light of the amendment of the Specification to incorporate the narrative from the applications incorporated by reference, thus providing antecedent basis for the claim limitations recited in claims 56-64.. See 37 CFR 1.75(d) (1) and MPEP § 608.01(o).

3. Withdrawn Claims 1, 2, 7, 36-38,45-49, and 56-64 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is herein withdrawn in light of the quotations marks having been removed from the claim. "identifying the presence of the one or more different pathogens in the stool sample as a biomarker that indicates that the individual has autism."

4. **Withdrawn** Claims 62-64 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (New Matter). The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 62-64 require that the individual further exhibits one or more symptoms of autism (thereby indicating that the claimed methods are relying on the presence of such additional symptoms as additional factors in the diagnosis of Autism). This rejection is herein withdrawn in light of the amendment of the Specification at page 2, which provides support for the claim limitations set forth in claims 62-64, the amendment being supported by applications 09/466,559 and 09/707,395 both of which are incorporated by reference into the instant Specification when originally filed.

Response to Arguments

5. Applicant's arguments with respect to claims 1, 2, and 7 , 36-38, 45-49, 56-67 have been considered but are moot in view of the new ground(s) of rejection. Various arguments will be addressed under the reformatted rejection of the claims under 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 2, and 7 , 36-38, 45-49, 56-67are rejected under 35 U.S.C. 112, first paragraph, because the specification, while apparently being enabling for diagnosing autism, by detecting the presence of antigens from a plurality of pathogens listed, for example, in Figure 3 or on page

9 of the application together with measuring abnormally low levels of chymotrypsin (page 10, instant Specification)in a child that exhibits characteristic behavioral symptoms of Autism, does not reasonably provide enablement for methods of such diagnosis by detecting antigens of a plurality pathogens.

7. It is noted that the claims have been amended or drafted to limit them to the detection of specific pathogenic antigens, the presence of which would be (according to the claim) indicative of the presence of, or potential for the development of, autism. However, rather than requiring the presence of each of the indicated infections, the claims have been amended to indicate that the mere detection of only two or more of the pathogens (such as H. pylori) would be indicative of autism (or the development of the disorder) in the patient.

8. As was indicated in the actions mailed on July 30, 2002 and July 29, 2003, the evidence provided by the Applicant does not demonstrate a clear correlation between the presence of the indicated pathogens and autism, as well as evidence provided by newly cited references to:

- Skeels et al (1990) who show children co-infected with Cryptosporidium and Giardia or E. histolytica which were not autistic, and were treated as transient infections without hospitalization (see page 306, col. 2, paragraph 3) and were not indicated to have autism;
- Nevo et al, (1997) shows individuals infected with both Campylobacter jejuni and Helicobacter pylori to evidence symptoms of acute immune polyneuropathy (title, abstract, Table 1, page S155) but do not have autism;
- Garcia et al (2000) show individuals infected with multiple parasites (title, abstract) to include Cryptosporidium, Giardia and/or E. histolytica (see page 3338, col. 1, paragraph 2, second to last sentence), but do not have autism.

- Peters et al 1986, show individuals stool samples with evidence of infection with both Entamoeba histolytica and Giardia (page 684, col. 2, paragraph 2) or Cryptosporidium and E. histolytica (page 685, col. 1, paragraph 3), and while the individuals have autoimmune disease, they do not have Autism.

9. As indicated in the prior actions, the teachings of the present application indicate that persons with Autism tend to have infectious by multiple pathogens. However, the teachings of the application also indicate that the specific pathogens present in autistic patients vary from person to person. There is no demonstration that the presence of antigens from any combination of pathogens would tend to indicate the presence of future potential for developing autism (see references cited above).

Moreover, with respect to the elected species of H. pylori, it is further noted that the art indicates that the presence of this pathogen may be indicative of other disorders than autism. See e.g., action mailed in July 2003, pages 10-11 and Nevo et al, 1997 (acute immune polyneuropathy, cited herein).

The instant Specification does teach children with abnormally low levels of chymotrypsin together with multiple pathogen infections are predisposed to Autism or have autism. The instant claims do not measure abnormally low levels of chymotrypsin in a sample for the same individual. The administration of digestive enzymes in claims 56-61 and 65-67 is not based upon the presence of abnormally low levels of chymotrypsin, nor any other digestive enzyme but the claims arbitrary administer digestive enzymes, and therefore do not require the individual to have abnormally low levels of any digestive enzyme.

Claims 62-64 each require that the individual "further exhibits one or more symptoms of autism" . However, it is noted that autistic disorders are diagnosed on the basis on the presence of multiple symptoms, wherein the mere presence of a single symptom would not appear to be indicative of the presence or development of the disorder. See e.g., Filipek et al., J Autism Dev Disord 29:439-84 (esp. pages 443-46), and Happy et al., Brain, 119:1377-400, at 1379 (indicating that autism and other PDDs require the presence of serious impairments in more than one area of development- i.e. requiring the presence of multiple "symptoms" of autism).

Thus, in view of the lack of correlation of the presence of any two of the indicated infections with autism, and the fact that no single symptom of autism would be sufficient to diagnose the presence of the disorder, there is no indication that the combination of the presence of two pathogens, and one symptom of autism would be diagnostic elements that would correlate with a clinical diagnosis of autism, these claims are not considered to overcome the enablement problems of the independent claims.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 56-61 and 65-67 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: ------- measuring chymotrypsin digestive enzyme levels in a sample from said individual, and administering to said individual a composition comprising chymotrypsin when chymotrypsin levels are abnormally low (support found on page 10 of the instant Specification paragraph 3)-------. Claims 56-61 and new claims 65-67

administer digestive enzymes to an individual but the individual is not so claimed as to be deficient in digestive enzymes, nor do the claimed methods' diagnose the presence of abnormally low levels of digestive enzymes in the individual of the claims. The source of the digestive enzymes is not claimed to be human or mammalian, but any type of digestive enzymes can be administered. Claims 65-67 recite the term "protease"; stool pathogens produce proteases such as Clostridial proteases that cause damage to the intestine. Claims 56-61 and 65-67 are incomplete, and do not distinctly, nor clearly claim Applicant's invention. See In re Mayhew, 1988.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 1,2,7, 45, 47-49 are rejected under 35 U.S.C. 102(a) as being anticipated by Reiter (WO01/27612, publication date April 19, 2001) in light of English translation provided by US Patent 7,129,053 (citations taken from US Pat.).

Reiter et al disclose the instantly claimed method that comprises the steps of:

Obtaining a stool sample from an individual(see abstract)

Analyzing the stool sample for the presence or absence of one or more antigens associated with two or more pathogens, specifically Helicobacter pylori and Campylobacter (jejuni) (see col. 1, lines 30-33) by performing a stool immunoassay (col. 4, lines 66-67).

Determining the presence of antigens associated with two or more different pathogens (see abstract "at least two"). With respect to applicant's newly added limitation of "determining that the individual has Autism based on the presence of the antigens associated with two or more different pathogens in the stool sample" (e.g., see claim 1)", the following is noted.

Regarding the "determining" step or clause recited in representative claim 1, it is noted that this "determining" step or clause does not recite any additional active method steps, but simply states a characterization or conclusion of the results of those steps or may be performed entirely in the human mind is obviously not tied to any machine and does not transform any article into a different state or thing. Therefore, the "determining" step or clause is not found to further limit the method defined by the claims, since it simply expresses the intended result of a process step positively recited (e.g. obtaining, analyzing). Given the broadest reasonable interpretation of the claims, the "determining" step simply reads on noticing, perceiving and/or looking at analysis results of the stool sample by a person, including the patient or a physician.

The mental step of "determining" does not negate the transformative steps of obtaining and analyzing, but has been given proper patentable weight in light of the statements noted herein.

Even though the claims are limited by and defined by the process, determination of patentability is based on the "obtaining and analyzing" steps. The patentability of the claimed methods does not depend on the step of "determining".

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001) Also, a species will anticipate a claim to a genus. See MPEP 2131.02.

Reiter et al inherently anticipates the instantly claimed invention as now claimed. because the reference carries out the claimed methods steps of obtaining a stool sample and analyzing the sample for two the claimed pathogens by immunoassay.

1. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. The Court further held that this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

14. Claims 1-2, 36-37, 45-46, 47, 48, 62-64 are rejected under 35 U.S.C. 102(e) as being anticipated by Feinberg et al (US PG-Pub 2008/0254009, effective filing date June 5, 2000).

15. The instant claims evidence the effective filing date of *November 16, 2001* in light of the recitation of Campylobacter and Clostridium difficile in all of the claims, and these claim limitations do not evidence original descriptive support in the earliest filed provisional application to which the instant application claims priority.

Feinberg et al disclose the instantly claimed invention directed to a method of determining, determining the risk or diagnosing [0009 "detecting a neurological or gastrointestinal disorder that has as an etiological component a microbe"] Autism in an individual (see [0014 early or late onset Autism], the method comprising the steps of:

Obtaining a stool (fecal) sample from an individual [0023, bottom half of paragraph],that is a child [0082, last line and Table 5], wherein the individual exhibits one or more symptoms of Autism (see [0056-0057, 0070] "Symptoms include loss of language, social and play skills, and onset of autistic characteristics such as avoidance of eye contact, self-stimulation behaviors"…. "genetic underpinnings", "infant-botalism")

Analyzing the stool sample for the presence or absence of Clostridium difficile [0020-0021] and Cryptosporidium [0012, 0017, 0020, 0074] by immunoassay[0023-0024], as well as additional pathogens to include Enterobacteriaceae (Table 5),

Determining, determining the risk(late onset[0014]), or diagnosing the presence of Autism based upon immunoassay[0023] analysis of the stool sample from the individual [0009, 0014].

Feingold anticipates the instantly claimed invention as now claimed.

Conclusion

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Various references are being cited to show co-infection by two pathogens and the medical conditions associated therewith.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Acting supervisor, Patricia Duffy can be reached on 571-272-0855. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ginny Portner/
Examiner, Art Unit 1645
October 26, 2010

/Mark Navarro/
Primary Examiner, Art Unit 1645